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Veterinary Vaccinology

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TABLE 4

Peptide vaccines for Parvo virus

	Antiviral activity*			Protection in target animals**		
	ELISA	NT	T cell	single dose	Double dose	Control
Langeveld et al. (1994)	+	+/-	-	1/6	9/9	0/4
Langeveld et al. (in prep.)	+	-	nt		nt	0/6

*nt = Not tested; + = activity present; - = no activity; +/- = activity in some individual animals.

**Ratio = number of protected animals/number of total animals.

which is shown to be highly conserved between strains and types, a peptide has been defined which readily induces full protection against disease in dogs after CPV infection using two vaccinations. Mink were protected with the same peptide vaccine against another parvovirus (mink enteritis virus) after a single vaccination. This appears to be the first example of a peptide vaccine which seems as effective as the classical vaccine based on whole virus.

9.5. CONCLUSION

From this, we speculate that it will be possible to develop effective peptide vaccine against other DNA viruses, notably those depending on humoral immunity for protection.

We further speculate that full protective peptide vaccines as effective as classical ones, are feasible in case of RNA viruses, like FMDV, if, in addition to the loop-peptide a peptide can be defined and constructed which represents one of the additional discrete neutralizing antigenic sites of FMDV.

PART 10. OTHER TYPES OF VACCINES (i.e., WITH CYTOKINES)

W. Strube

The immune response can be divided into two functional groups: the innate or primitive immune system and the adaptive immune system (Büttner, 1993). The innate immune system, which represents the first barrier in the combat against infectious diseases, is mediated by antigen non-specific actions of neutrophils, natural killer cells, macrophages and by soluble factors like the complement system. The adaptive immune system is represented by the antigen-specific B- and T-cells. Both parts of the immune response are modulated by, and interact through, cytokines, including interleukins (IL), interferons (IFN), colony stimulating factors (CSF) and tumour necrosis factors (TNF) (Roitt et al., 1989). IL-1 is synthesized by antigen-presenting cells and contribute to T- and B-cell stimulation (Mizel, 1982). IL-2, IL-4, IL-5, and IFN-gamma are involved in clonal proliferation and differentiation of immune cells (Kelso, 1989; O'Garra et al., 1988). IL-2 contributes especially to proliferation, differentiation and cytotoxic activity of T-cells (Farrar et al., 1982). IFN-gamma stimulates macrophages and induces expression of MHC class II (Roitt et al., 1989). Due to their physiological function in the immune system cytokines,

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when combined or applied simultaneously with immunogens, may influence immunogenicity of vaccines. Therefore, cytokines were evaluated as 'natural' adjuvants in various vaccine models. Schijns and co-workers compared different cytokines in a rabies challenge model in mice (Schijns et al., 1994). Whereas TNF-alpha and IL-1-alpha, when applied shortly before rabies vaccination only marginally induced protection against challenge infection, IFN-gamma and IL-2, respectively, markedly increased immunogenicity following vaccination. Combined administration of IFN-gamma and IL-2 synergistically enhanced formation of neutralizing antibodies following rabies vaccination but did not further increase resistance to challenge. Reddy and colleagues reported that administration of recombinant bovine IL-1 β in combination with a BHV-1 live attenuated vaccine increased the vaccine induced cytotoxic immune response in cattle and reduced challenge virus replication following experimental infection (Reddy et al., 1990). The same team also tested recombinant bovine IL-2 as an adjuvant of a live BHV1 vaccine (Reddy et al., 1989). Five consecutive applications of IL-2 significantly enhanced humoral and cellular immune responses as well as clinical protection following immunization with a live attenuated BHV1 vaccine in cattle. No additive effect was observed when IL-1 and IL-2 were administered together (Reddy et al., 1993). Hughes and co-workers confirmed the efficacy of IL-2 in cattle and demonstrated that multiple injections of IL-2 following vaccination with a BHV1 glycoprotein gD vaccine significantly increased BHV1 specific cytotoxicity and gD specific lymphocyte proliferation response compared to vaccinated animals that were not treated with IL-2 (Hughes et al., 1991). In the ovine system, IL-1 and 2, as well as TNF, have been produced by recombinant DNA techniques (Fash et al., 1993). Adjuvant studies using avidin as a model antigen demonstrated that ovine IL-1 significantly increased antibody formation in sheep (Andrews et al., 1994). The use of cytokines as natural adjuvants may even allow the stimulation of specific immunoglobulin classes. The use of a recombinant vaccinia virus expressing murine IL-5 and influenza HA protein demonstrated that IL-5 selectively enhanced mucosal IgA response specific for HA in mice (Ramsay and Kohonen-Corish, 1993). In summary, all these results indicated that cytokines may indeed be used to improve efficacy of vaccines. Babiuk's group has already constructed a molecular chimera of a *Pasteurella haemolytica* leukotoxin and IL-2 (Hughes et al., 1992). Because of safety, efficacy and manufacturing aspects, such antigen-cytokine complexes may represent future vaccines.

PART 11. FUTURE TYPES OF VACCINATION

R.H. Meloen

This section deals with most of the veterinary vaccines we may expect in the future. Presently, two sorts are emerging: one that deals with vaccines against 'self' protein, notably hormones. These vaccines will be dealt with elsewhere. The other one deals with DNA vaccination.

11.1. DNA VACCINATION

DNA plasmids can be used for DNA vaccination (Davis et al., 1993; Robinson et al., 1993) and have a number of appealing advantages: large proteins can be easily expressed in eukaryotic cells, vaccine design is relatively easy, the vaccine itself is